Small Molecules to inhibit Nemo-like Kinase for Treatment of Diamond Blackfan Anemia

Grant Award Details

Small Molecules to inhibit Nemo-like Kinase for Treatment of Diamond Blackfan Anemia

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-12475

Project Objective: To identify a small molecule NEMO-like kinase inhibitor for treating Diamond Blackfan Anemia (DBA).

Investigator:

Name:	Kathleen Sakamoto
Institution:	Stanford University
Type:	PI

Disease Focus: Anemia, Blood Disorders

Human Stem Cell Use: Adult Stem Cell, iPS Cell

Award Value: $848,098

Status: Active

Grant Application Details

Application Title: Small Molecules to inhibit Nemo-like Kinase for Treatment of Diamond Blackfan Anemia

Public Abstract:

Research Objective

We propose to study small molecules that inhibit Nemo-like Kinase, to improve the production of red blood cells in bone marrow stem cells of children with Diamond Blackfan Anemia (DBA).

Impact

If small molecule NLK inhibitors are identified that are effective in improving the anemia of DBA and nontoxic, then treatment and transfusions would not be necessary.

Major Proposed Activities

- Treat RPS19 and RPL11 knockdown and normal human cord blood hematopoietic stem cells (HSC) with NLK inhibitors in vitro. (Months 0-2)
- Treat HSC from transgenic mice with inducible RPS19 and RPL11 knockdown or normal mice with OTS167 in vitro. (Months 2-6)
- Treat mice with RPS19 and RPL11 in stem cell transplant models to determine the efficacy of OTS167 in vivo. (Months 4-18)
- Determine the toxicity of OTS167 in normal mice. (Months 6-12)
- Study the molecular pathways downstream of OTS167 by RNA-seq and Cytometry Time of Flight (CyTOF) in human cord blood HSC (Months 12-24).
- Perform experiments to test with other potential small molecules that target NLK. (Months 20-24).

Statement of Benefit to California:

Development of small molecules to inhibit NLK in DBA would result in a significant improvement in the quality of life in these patients. Although DBA is a rare disease, this treatment could also benefit patients with a subtype of myelodysplastic syndrome with del(5q). Development of novel NLK inhibitors could result in a new startup companies, licensing, and create new job opportunities for individuals who live in California.
